UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,457	11/13/2000	ANTONI BANAS	P04962US/UA/MW	4182

466 7590 12/02/2002

YOUNG & THOMPSON
745 SOUTH 23RD STREET 2ND FLOOR
ARLINGTON, VA 22202

EXAMINER	
KALLIS, RUSSELL	
ART UNIT	PAPER NUMBER
1638	12

DATE MAILED: 12/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/709,457	BANAS ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5 and 6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, Claims 1-9 in Paper No. 11 is acknowledged.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims a nucleic acid sequence encoding an enzyme catalyzing the transfer of a fatty acid from acyl-CoA to diacylglycerol for the production of triacylglycerol, a nucleic acid sequence derived from SEQ ID NO: 1, a nucleic acid sequence derived from the *Saccharomyces cerevisiae ARE1* genomic or cDNA clone, and a nucleic acid sequence or cDNA encoding a protein having 60% or more sequence identity to the amino acid sequence of SEQ ID NO: 2.

Applicant describes the nucleic acid of SEQ ID NO: 1 encoding the amino acid of SEQ ID NO: 2.

Applicant does not describe sequences other than SEQ ID NO: 1 and 2, any other sequences that are a nucleic acid sequence or fragments encoding an enzyme catalyzing the

transfer of a fatty acid from acyl-CoA to diacylglycerol, derivations thereof, the *ARE1* gene from yeast and derivations thereof, and nucleic acid sequence encoding an amino acid sequence having 60% sequence identity to SEQ ID NO: 2.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the claimed invention.

See *University of California V. Eli Lilly and Co.,* 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

Given the failure of a nucleic acid sequence or fragments encoding an enzyme catalyzing the transfer of a fatty acid from acyl-CoA to diacylglycerol and derivations thereof, the *ARE1* gene from yeast and derivations thereof, and nucleic acid sequence encoding an amino acid sequence having 60% sequence identity to SEQ ID NO: 2 to be adequately described, methods of its use are also inadequately described. See Written Description Guidelines, Federal Register Vol. 66 No. 4, Friday January 5, 2001 "Notices", pages 1099-111.

3. Claim 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for increasing TAG and oil levels in yeast and *Arabidopsis* transformed with SEQ ID NO: 1 or with the native ARE1 gene from yeast, does not reasonably provide enablement for any organism transformed with any nucleic acid sequence encoding an amino acid that catalyzes the transfer of a fatty acid from acyl-CoA to diacylglycerol for the production of TAG thereby increasing the oil content of said transgenic organism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant broadly claims a nucleic acid sequence or gene fragments and derivations thereof encoding an enzyme catalyzing the transfer of a fatty acid from acyl-CoA to diacylglycerol, the *ARE1* gene from yeast and derivations thereof, and nucleic acid sequences encoding an amino acid sequences having 60% sequence identity or more to SEQ ID NO: 2; methods of using said sequences to increase the level of TAG and oil in an organism; recombinant transfer and expression of said sequences to increase the level of oil in a eukaryotic organism (fungi, plants, and animals); recombinant transfer and expression of said nucleic acid sequences under control of a storage organ specific promoter or a seed-specific promoter in an agricultural plant whereby the TAG and oil content is increased.

Applicant teaches disruption of the ARE1 gene in yeast and a reduced accumulation of TAG by 40% when compared to wild type yeast (Example 1 pages 6-9); yeast transformed with and overexpressing the ARE1 gene having increased TAG or oil levels (Example 2 pages 9-10); diacylglycerol acyltransferase activity, measured as radiolabelled TAG production, in microsomal fractions prepared from wild type and mutant (*are1*) yeast cells transformed with a

plasmid encoding ARE1 (Example 3 pages 11-12); *Arabidopsis* transformed with and expressing the ARE1 gene from yeast having increased TAG or oil levels (Example 4 pages 13-14).

Applicant does not teach the use of any other nucleic acid sequence or fragment capable of expressing an amino acid that catalyzes the transfer of a fatty acid from acyl-CoA to diacylglycerol producing TAG and increasing the oil content of said organism from any DNA sequence derived from SEQ ID NO: 1, or derived from the yeast *ARE1* gene, or any nucleic acid encoding an amino acid having 60% sequence identity with SEQ ID NO: 2; or any other organisms, agricultural or otherwise, transformed with said sequences having increased oil content other than yeast and *Arabidopsis* transformed with SEQ ID NO: 1.

The isolation of orthologous DNA sequences from other species encoding the same catalytic activity introduces an element of unpredictability. The limitation is introduced in finding homologous regions that would adequately enable either PCR amplification or southern hybridization and would entail using either degenerate primers or probes with limited homology. Thus the screen for orthologous sequences would isolate many genes other than those of interest.

Unpredictability is exemplified in the example of isolating DNA fragments where using stringent hybridization conditions did not always select for homologous DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single

nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2).

Further, the inherent unpredictability in isolation of a homologous sequence encoding the same protein activity is illustrated in an example where a small number of changes to the coding region for a strict desaturase resulted in an enzyme with a hydroxylase activity and that a small number of changes to the coding region of a desaturase could account for the functional divergence seen across a range of enzymes involved in fatty acid metabolism (Broun *et al.* Science Vol. 282 13 November 1998; Abstract lines 4-6 and p. 1317 column 1, lines 51-56).

The unpredictability inherent in transforming with a homologous inter-functional 5' UTR regulatory gene sequence is exemplified in the loss of heritable activity of a target gene regulated by a promoter inserted into a genome already containing a homologous endogenous copy of that promoter (i.e. a tissue specific or organ specific promoter) and cannot be anticipated with any reasonable degree of predictability (Park Y. D. *et al.,* Plant Journal 1996, Feb. 9, (2): 183-194, see Abstract).

Because the specification provides no guidance for amplifying to isolate unknown diacylglycerol acyltransferase genes using degenerate PCR primers, one of skill in the art would be required to optimize PCR conditions to eliminate non specific binding and the artifacts generated thereof. This would comprise adjustments in annealing temperatures, testing different concentrations of Mg and template, and the sequencing of putative clones for each species of diacylglycerol acyltransferase cDNA amplified to verify the product as an diacylglycerol

acyltransferase. The unpredictability in the art would require screening numerous non-exemplified transgenic plants to test various non-exemplified diacylglycerol acyltransferase constructs for effectively modified plants and seeds with increased oil levels presuming they could ever be obtained in every plant species claimed.

Given the lack of guidance for isolating DNA sequences encoding an diacylglycerol acyltransferase and producing agricultural plants and other organisms transformed to have increased oil production in the specification; that reflect the breadth of the claims, and given the unpredictability in the art, undue trail and error experimentation would be needed by one skilled in the art to isolate a multitude of non-exemplified diacylglycerol acyltransferase genes, or to evaluate the ability of a multitude of non-exemplified diacylglycerol acyltransferase genes or non-exemplified gene products to alter the phenotype of a multitude of transformed plant species or in other organisms including animals. Therefore, the invention is not enabled for the scope set forth in the claims.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in the rejection.

At Claims 2 and 3, line 1, "is derived from" is indefinite. It is unclear how the sequence is to be derived and what has changed from the original sequence.

Claims 1-4 provide for the use of a nucleic acid, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is

intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The oil producing organism of Claim 1 and dependent Claims 2-6 as well as the transgenic organisms of Claims 5-6 encompass transformation of humans and transformed humans. See *American Wood v. Fiber Distintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Lardizabal K. *et al.*, WO 98/55631A1 published December, 10 1998.

The claims are indefinite as discussed supra, specifically nucleic acid sequence derived from SEQ ID NO: 1 or the ARE1 gene from yeast read upon any other nucleic acid sequences having diacylglycerol acyltransferase activity.

The claims are broad for reasons discussed supra, specifically with respect to a nucleic acid encoding an amino acid with the activity of catalyzing the transfer of a fatty acid, i.e. an acyl group, from an acyl-CoA to diacylglycerol for the production of triacylglycerol wherein said sequence is derived from SEQ ID NO: 1 or is derived from the *ARE1* gene of yeast or encodes a protein with 60% sequence identity or more to SEQ ID NO: 2.

Lardizabal teaches that flux into glycerol lipids is controlled by diacylglycerol acyltransferase converting DAG into TAG and its usefulness in increasing oil production in a plant on page 3 line 22 to page 4 line 24; agricultural plants useful for increasing oil production in a plant transformed with a nucleic acid sequence encoding an amino acid expressing a diacylglycerol acyltransferase on page 22 lines 14 to 36; techniques useful for isolating diacylglycerol acyltransferase (DAGAT) genes; and the usefulness of seed specific napin and oleosin promoters for increasing oil production in seeds. Thus the reference teaches all the limitations of Claims 1-9.

11. All claims are rejected.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the legal analyst, Gwendolyn Payne, whose telephone number is (703) 305-2475.

Russell Kallis Ph.D.
November 26, 2002

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638